

NMCP COVID-19 Literature Report #67: Friday, 07 May 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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The Big Picture

News in Brief

"A new analysis of the toll of the Covid-19 pandemic suggests 6.9 million people worldwide have died from the disease, more than twice as many people as has been officially reported" ([STAT](#)).

"How did the covid-19 outbreak in India get so bad?" ([WP](#))

Experts now think that 'herd immunity' is unlikely—'persistent hesitancy' and variants are working against it ([NYT](#)).

Series: "After the virus: How COVID-19 changed the US military forever" ([Military.com](#)).

"'Unprecedented achievement': who received the first billion COVID vaccinations? It took just four months to reach this global milestone, and hitting to the two-billion mark could happen even faster, say scientists" ([Nature](#)).

Special Reports and Other Resources

RAND: [Superspreaders of Malign and Subversive Information on COVID-19. Russian and Chinese Efforts Targeting the United States](#) (29 April 2021)

"The global spread of coronavirus disease 2019 (COVID-19) created a fertile ground for attempts to influence and destabilize different populations and countries. Both Russia and China appear to have employed information manipulation during the COVID-19 pandemic in service to their respective global agendas. This report uses exploratory qualitative analysis to systematically describe the types of COVID-19-related malign and subversive information efforts with which Russia- and China-associated outlets appear to have targeted U.S. audiences from January 2020 to July 2020 and organizes them into a framework. This work lays the foundation for a better understanding of how and whether Russia and China might act and coordinate in the domain of malign and subversive information efforts in the future. This report is the first in a series that will use big data, computational linguistics, and machine learning to test findings and hypotheses generated by the initial analysis.

This report is part of RAND's Countering Truth Decay initiative, which considers the diminishing role of facts and analysis in political and civil discourse and the policymaking process. Disinformation and its rampant spread online and offline is one of the key drivers of Truth Decay. Agents—notably such foreign actors as Russia and China and their proxies—fuel and contribute to the explosion in disinformation observed over the past decade. Knowing how Russia and China operate in this space can help inform our understanding of the Truth Decay phenomenon and efforts to mitigate it.

Key Findings

- Both countries disseminated messages through a wide variety of channels and platforms, including social media.
- Both countries attempted to tarnish the reputation of the United States by emphasizing challenges with its pandemic response and characterizing U.S. systems as inadequate.
- Both countries falsely accused the United States of developing and intentionally spreading the virus.
- The two countries appeared to differ in their principal goals for COVID-19-related information efforts: Russia aimed to destabilize the United States; China aimed to protect and enhance its own international reputation.
- Both countries modified their COVID-19-related messaging over time, focusing on conspiracy theories about the virus's origins and impacts from March 2020 to April 2020 and later moving to concentrate on perceived U.S. failure in responding to the pandemic.
- While Russia deployed media with wide-ranging ideologies and a variety of audiences, China-linked messaging was ideologically uniform, consistent across multiple information outlets, and appeared to target audiences that were less varied.
- Countering apparent Russian and Chinese malign and subversive information efforts will require campaigns that consider the capabilities and thematic emphasis of each of these actors.
- Profiling Russian and Chinese sources known to frequently create and disseminate disinformation and propaganda can also inform counter-messaging efforts.
- China and Russia appear to amplify one another's messages, when opportune. This might eventually lead to some collaboration, albeit limited in nature.
- Public health messaging should account for potential impacts of Russian and Chinese messaging on vaccination uptake."

Peer-Reviewed Articles

MMWR: [Modeling of Future COVID-19 Cases, Hospitalizations, and Deaths, by Vaccination Rates and Nonpharmaceutical Intervention Scenarios — United States, April–September 2021](#)
(05 May 2021)

"What is already known about this topic? Increases in COVID-19 cases in March and early April occurred despite a large-scale vaccination program. Increases coincided with the spread of SARS-CoV-2 variants and relaxation of nonpharmaceutical interventions (NPIs).

What is added by this report? Data from six models indicate that with high vaccination coverage and moderate NPI adherence, hospitalizations and deaths will likely remain low

nationally, with a sharp decline in cases projected by July 2021. Lower NPI adherence could lead to substantial increases in severe COVID-19 outcomes, even with improved vaccination coverage.

What are the implications for public health practice? High vaccination coverage and compliance with NPIs are essential to control COVID-19 and prevent surges in hospitalizations and deaths in the coming months."

JAMA Netw Open: [Trends in Patient Characteristics and COVID-19 In-Hospital Mortality in the United States During the COVID-19 Pandemic](#) (03 May 2021)

"Question What factors are associated with observed trends in the in-hospital mortality rates in the United States during the first 9 months of the COVID-19 pandemic?

Findings In this cohort study of 20 736 patients, in-hospital mortality rates decreased in the US between March and November 2020, even after accounting for the changing mix in patient age, sex, comorbidities, and disease severity at the time of admission. Hospital and intensive care unit length of stay and use of mechanical ventilation decreased over time, whereas the use of glucocorticoids and remdesivir increased.

Meaning Changes in age, sex, comorbidities, and disease severity among patients with COVID-19 do not fully explain the decrease in the in-hospital mortality rates observed during the first 9 months of the COVID-19 pandemic."

Intensive Care Med: [Evolving changes in mortality of 13,301 critically ill adult patients with COVID-19 over 8 months](#) (14 April 2021)

"Purpose: Clinical characteristics and management of COVID-19 patients have evolved during the pandemic, potentially changing their outcomes. We analyzed the associations of changes in mortality rates with clinical profiles and respiratory support strategies in COVID-19 critically ill patients.

Methods: A multicenter cohort of RT-PCR-confirmed COVID-19 patients admitted at 126 Brazilian intensive care units between February 27th and October 28th, 2020. Assessing temporal changes in deaths, we identified distinct time periods. We evaluated the association of characteristics and respiratory support strategies with 60-day in-hospital mortality using random-effects multivariable Cox regression with inverse probability weighting.

Results: Among the 13,301 confirmed-COVID-19 patients, 60-day in-hospital mortality was 13%. Across four time periods identified, younger patients were progressively more common, non-invasive respiratory support was increasingly used, and the 60-day in-hospital mortality decreased in the last two periods. 4188 patients received advanced respiratory support (non-invasive or invasive), from which 42% underwent only invasive mechanical

ventilation, 37% only non-invasive respiratory support and 21% failed non-invasive support and were intubated. After adjusting for organ dysfunction scores and premorbid conditions, we found that younger age, absence of frailty and the use of non-invasive respiratory support (NIRS) as first support strategy were independently associated with improved survival (hazard ratio for NIRS first [95% confidence interval], 0.59 [0.54-0.65], $p < 0.001$).

Conclusion: Age and mortality rates have declined over the first 8 months of the pandemic. The use of NIRS as the first respiratory support measure was associated with survival, but causal inference is limited by the observational nature of our data."

SARS-CoV-2 Variants

News in Brief

"Will Covid-19 vaccines protect you against variants? 9 questions about variants, answered. How coronavirus variants are affecting vaccines, treatments, and our attempts to return to normal" ([Vox](#)).

Add otters to list of non-human critters that can be infected with SARS-CoV-2: Two otters at an aquarium in Georgia were checked after showing clinical signs including sneezing, runny noses, and coughing ([USDA](#); see also: [cases of SARS-CoV-2 in animals in the US](#)).

Peer-Reviewed Articles

MMWR: [Rapid Emergence and Epidemiologic Characteristics of the SARS-CoV-2 B.1.526 Variant — New York City, New York, January 1–April 5, 2021](#) (05 May 2021)

"What is already known about this topic? B.1.526 emerged in November 2020 as a SARS-CoV-2 variant of interest in New York City (NYC). The presence of the E484K mutation is concerning because it has been shown to attenuate antibody neutralization in vitro.

What is added by this report? The NYC Department of Health and Mental Hygiene analyzed laboratory and epidemiologic data to characterize cases of B.1.526 infection and the associated potential for breakthrough infection and reinfection. Preliminary evidence suggests that, to date, B.1.526 does not lead to more severe disease or increased risk for infection after vaccination.

What are the implications for public health practice? Rapid integration of whole genome sequencing and population-based surveillance data is critical to characterizing new SARS-CoV-2 variants."

JAMA: [US Case Reports of Cerebral Venous Sinus Thrombosis With Thrombocytopenia After Ad26.COV2.S Vaccination, March 2 to April 21, 2021](#) (30 April 2021)

"Question What were the clinical characteristics of the first US patients reported to have cerebral venous sinus thrombosis (CVST) with thrombocytopenia following receipt of the Ad26.COV2.S (Janssen/Johnson & Johnson) COVID-19 vaccine?

Findings In this case series of 12 patients, all were women, younger than 60 years, and had symptom onset ranging from 6 to 15 days after vaccination requiring hospitalization. Of 11 patients with heparin-platelet factor 4 enzyme-linked immunosorbent assay (ELISA) heparin-induced thrombocytopenia (HIT) antibody test results, all were positive. At last follow-up, outcomes were death (n = 3), intensive care unit (ICU) care (n = 3), non-ICU hospitalization (n = 2), and discharge to home (n = 4).

Meaning This case series may inform clinical guidance and investigations into the potential relationship between the Ad26.COV2.S vaccine and CVST with thrombocytopenia."

MMWR: [COVID-19 Outbreak Associated with a SARS-CoV-2 R.1 Lineage Variant in a Skilled Nursing Facility After Vaccination Program — Kentucky, March 2021](#) (30 April 2021)

"What is already known about this topic? COVID-19 vaccines have demonstrated high efficacy in clinical trials. Limited data are available on effectiveness in skilled nursing facilities (SNFs) and against emerging variants.

What is added by this report? In a COVID-19 outbreak at a Kentucky SNF involving a newly introduced variant to the region, unvaccinated residents and health care personnel (HCP) had 3.0 and 4.1 times the risk of infection as did vaccinated residents and HCP. Vaccine was 86.5% protective against symptomatic illness among residents and 87.1% protective among HCP.

What are the implications for public health practice? Vaccination of SNF residents and HCP is essential to reduce the risk for symptomatic COVID-19, as is continued focus on infection prevention and control practices."

MMWR: [Linked Clusters of SARS-CoV-2 Variant B.1.351 — Maryland, January–February 2021](#) (30 April 2021)

"What is already known about this topic? In January 2021, a SARS-CoV-2 specimen from a Maryland resident was determined to be the B.1.351 variant, first identified in South Africa. The SARS-CoV-2 B.1.351 variant might elicit a reduced neutralizing antibody response.

What is added by this report? Investigation identified two linked clusters of SARS-CoV-2 infection, comprising 17 total patients (two were hospitalized and one died) who did not report recent travel. Four patients' specimens were sequenced; all were the B.1.351 variant.

What are the implications for public health practice? These were the first identified clusters of B.1.351 in the United States with no link to travel. Completed contact investigations, expanded genetic sequencing, and universal prevention strategies, including vaccination, masking, and distance, might prevent the spread of SARS-CoV-2 variants of concern, including B.1.351."

Vaccines and Vaccine Hesitancy

News in Brief

"Pfizer, BioNTech ask FDA for full approval of Covid-19 vaccine. If granted, the Pfizer vaccine would be the first in the U.S. to be fully approved" ([NBC](#)).

Booster shots may be in our future, especially for older adults or those with underlying conditions ([CNBC](#)).

Another option: vaccine mix and match to boost the immune system response ([NPR](#)).

The 'pause' on the J&J vaccine has been lifted ([CDC](#)).

Citing safety concerns, Brazil's Health Regulatory Agency rejected Russia's Sputnik V vaccine ([WP](#); for a deeper dive, see this [BuzzFeed article](#) or this [conversation with virologist Angela Rasmussen](#)).

The NIH will study COVID-19 vaccine responses in people with immune deficits or dysregulations ([NIH](#)).

Supply and Demand

The US will share up to 60 million doses of the AstraZeneca vaccine with other countries ([BBC](#)).

Together, CVS and Walgreens have wasted more than 125,000 doses of COVID-19 vaccine—more than U.S. states, territories, and government agencies combined. ([KHNN](#)).

Long read: "How Pfizer makes its Covid-19 vaccine" ([NYT](#); includes a lot of graphics and gifs).

Messaging

"Few would fear COVID vaccines if policy makers explained their risks better: Clear messaging and transparency are vital, say some experts on risk assessment and decision-making" ([Sci Am](#)).

One confounder for good messaging is the public's trust in the CDC has declined during the pandemic ([RAND](#)).

The newly launched 'We Can Do This' campaign is designed to increase confidence in COVID-19 vaccines and encourage vaccination ([HHS](#)).

Sesame Street is getting in on the action by developing videos to promote getting vaccinated ([NYT](#)).

Words matter: maybe we would be better off using 'community immunity' instead of 'herd immunity', or 'physical distancing' instead of 'social distancing' to avoid unconscious biases ([Twitter](#); medical librarian's personal opinion).

Hesitancy and Antivax

"Why Black and Latino people still lag on COVID vaccines — and how to fix it" ([NPR](#)).

"Anti-vaxxers aren't the cause of America's dropping vaccine rates: This fact is crucial to getting the US's vaccination campaign back on track" ([Vox](#)).

"Millions are saying no to the vaccines. What are they thinking? Feelings about the vaccine are intertwined with feelings about the pandemic" ([Atlantic](#); see also this [Atlantic article on COVID-19 denialism](#)).

"COVID vaccines: time to confront anti-vax aggression. Halting the spread of the coronavirus will require a high-level counteroffensive against new destructive forces" ([Nature](#)).

Misinformation

The J&J vaccine pause created a perfect storm for misinformation ([NPR](#)).

"The anti-vaccine influencers who are merely asking questions: Institutional experts haven't adapted to today's media ecosystem. Other commentators are filling the gap" ([Atlantic](#)).

Webinar

WHEN: Wednesday, 12 May 2021, 1330 ET

WHAT: Be a COVID-19 Vaccine Champion

DETAILS: "As healthcare and public health systems continue vaccinating community members against COVID-19, there is a need to provide information that builds confidence and helps people make informed decisions about the vaccines. ASPR TRACIE, in collaboration with New York City Health + Hospitals, is hosting the "Be A COVID-19 Vaccine Champion" webinar where speakers will discuss this local initiative dedicated to building confidence in the vaccines; provide information about the current FDA authorized COVID-19 vaccines and their safety and effectiveness; and share effective communication strategies to encourage friends, family, colleagues, and the community to get vaccinated. Additional educational resources and tools developed by local healthcare partners will be shared. There will also be significant time provided for participant Q&A."

REGISTER: <https://register.gotowebinar.com/register/1305226269799911695>

Special Reports and Other Resources

TML: [COVID-19 Vaccine Comparison Chart \[pdf\]](#) (updated 26 April 2021)

This table includes information on type, age, dosage, efficacy, and safety on the various COVID-19 vaccines from Pfizer/BioNTech, Moderna, J&J (Janssen), AstraZeneca, and Novavax.

Peer-Reviewed Articles

JAMA: [Association Between Vaccination With BNT162b2 and Incidence of Symptomatic and Asymptomatic SARS-CoV-2 Infections Among Health Care Workers](#) (06 May 2021)

"Question What is the association between receipt of the Pfizer-BioNTech BNT162b2 vaccine and the incidence of symptomatic and asymptomatic SARS-CoV-2 infection among health care workers?

Findings In this retrospective cohort study conducted in Tel Aviv, Israel, that included 6710 health care workers who underwent periodic testing for SARS-CoV-2 infection, vaccination with the BNT162b2 vaccine was associated with an adjusted incidence rate ratio of 0.03 for symptomatic infection and 0.14 for asymptomatic infection more than 7 days after the second dose. Both incidence rate ratios were statistically significant.

Meaning Receipt of the BNT162b2 vaccine was significantly associated with lower incidence of symptomatic and asymptomatic SARS-CoV-2 infection among health care workers."

JAMA: [Asymptomatic and Symptomatic SARS-CoV-2 Infections After BNT162b2 Vaccination in a Routinely Screened Workforce](#) (06 May 2021)

"This study aims to describe an association between the Pfizer-BioNTech (BNT162b2) vaccine and decreased risk of symptomatic and asymptomatic infections with SARS-CoV-2 in hospital employees."

NEJM: [Efficacy of NVX-CoV2373 Covid-19 Vaccine against the B.1.351 Variant](#) (05 May 2021)

"In this phase 2a–b trial in South Africa, we randomly assigned human immunodeficiency virus (HIV)–negative adults between the ages of 18 and 84 years or medically stable HIV-positive participants between the ages of 18 and 64 years in a 1:1 ratio to receive two doses of either the NVX-CoV2373 vaccine (5 µg of recombinant spike protein with 50 µg of Matrix-M1 adjuvant) or placebo. The primary end points were safety and vaccine efficacy against

laboratory-confirmed symptomatic Covid-19 at 7 days or more after the second dose among participants without previous SARS-CoV-2 infection.

Of 6324 participants who underwent screening, 4387 received at least one injection of vaccine or placebo. Approximately 30% of the participants were seropositive for SARS-CoV-2 at baseline. Among 2684 baseline seronegative participants (94% HIV-negative and 6% HIV-positive), predominantly mild-to-moderate Covid-19 developed in 15 participants in the vaccine group and in 29 in the placebo group (vaccine efficacy, 49.4%; 95% confidence interval [CI], 6.1 to 72.8). Vaccine efficacy among HIV-negative participants was 60.1% (95% CI, 19.9 to 80.1). Of 41 sequenced isolates, 38 (92.7%) were the B.1.351 variant. Post hoc vaccine efficacy against B.1.351 was 51.0% (95% CI, -0.6 to 76.2) among the HIV-negative participants. Preliminary local and systemic reactogenicity events were more common in the vaccine group; serious adverse events were rare in both groups.

The NVX-CoV2373 vaccine was efficacious in preventing Covid-19, with higher vaccine efficacy observed among HIV-negative participants. Most infections were caused by the B.1.351 variant."

MMWR: [Safety Monitoring of the Janssen \(Johnson & Johnson\) COVID-19 Vaccine — United States, March–April 2021](#) (30 April 2021)

"What is already known about this topic? An Emergency Use Authorization of the Janssen COVID-19 vaccine was granted February 27, 2021. Use was paused during April 12–23, 2021, after detection of six cases of cerebral venous sinus thrombosis (CVST).

What is added by this report? By April 21, nearly 8 million doses of the Janssen COVID-19 vaccine had been administered. Review of safety monitoring data found that 97% of reported reactions after vaccine receipt were nonserious, consistent with preauthorization clinical trials data. Seventeen thrombotic events with thrombocytopenia have been reported, including three non-CVST events.

What are the implications for public health practice? Ongoing monitoring for rare and common adverse events after vaccination is important for evaluating the balance between risks and benefits for each authorized COVID-19 vaccine, including the Janssen COVID-19 vaccine."

MMWR: [Anxiety-Related Adverse Event Clusters After Janssen COVID-19 Vaccination — Five U.S. Mass Vaccination Sites, April 2021](#) (30 April 2021)

"What is already known about this topic? Syncope and other anxiety-related events can occur after vaccination and have been reported to the Vaccine Adverse Events Reporting System (VAERS) for other vaccines.

What is added by this report? Five mass vaccination sites reported 64 anxiety-related events, including 17 events of syncope (fainting) after receipt of Janssen COVID-19 vaccine. The reporting rates of syncope to VAERS after Janssen COVID-19 and influenza vaccines (2019–20) were 8.2 and 0.05 per 100,000 doses, respectively.

What are the implications for public health practice? Vaccine providers should be aware of anxiety-related events after vaccination and observe all COVID-19 vaccine recipients for any adverse reactions for at least 15 minutes after vaccine administration."

Science: [Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose](#) (30 April 2021)

"SARS-CoV-2 vaccine rollout has coincided with the spread of variants of concern. We investigated if single dose vaccination, with or without prior infection, confers cross protective immunity to variants. We analyzed T and B cell responses after first dose vaccination with the Pfizer/BioNTech mRNA vaccine BNT162b2 in healthcare workers (HCW) followed longitudinally, with or without prior Wuhan-Hu-1 SARS-CoV-2 infection. After one dose, individuals with prior infection showed enhanced T cell immunity, antibody secreting memory B cell response to spike and neutralizing antibodies effective against B.1.1.7 and B.1.351. By comparison, HCW receiving one vaccine dose without prior infection showed reduced immunity against variants. B.1.1.7 and B.1.351 spike mutations resulted in increased, abrogated or unchanged T cell responses depending on human leukocyte antigen (HLA) polymorphisms. Single dose vaccination with BNT162b2 in the context of prior infection with a heterologous variant substantially enhances neutralizing antibody responses against variants."

MMWR: [Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Among Hospitalized Adults Aged ≥65 Years — United States, January–March 2021](#) (28 April 2021)

"What is already known about this topic? Clinical trials suggest high efficacy for COVID-19 vaccines, but evaluation of vaccine effectiveness against severe outcomes in real-world settings and in populations at high risk, including older adults, is needed.

What is added by this report? In a multistate network of U.S. hospitals during January–March 2021, receipt of Pfizer-BioNTech or Moderna COVID-19 vaccines was 94% effective against COVID-19 hospitalization among fully vaccinated adults and 64% effective among partially vaccinated adults aged ≥65 years.

What are the implications for public health practice? SARS-CoV-2 vaccines significantly reduce the risk for COVID-19–associated hospitalization in older adults and, in turn, might lead to commensurate reductions in post-COVID conditions and deaths."

Clin Infect Dis: [Age-dependent immune response to the Biontech/Pfizer BNT162b2 COVID-19 vaccination](#) (27 April 2021)

"Background: The SARS-CoV-2 pandemic has led to the development of various vaccines. Real-life data on immune responses elicited in the most vulnerable group of vaccinees over 80 years old is still underrepresented despite the prioritization of the elderly in vaccination campaigns.

Methods: We conducted a cohort study with two age groups, young vaccinees below the age of 60 and elderly vaccinees over the age of 80, to compare their antibody responses to the first and second dose of the BNT162b2 COVID-19 vaccination.

Results: While the majority of participants in both groups produced specific IgG antibody titers against SARS-CoV-2 spike protein, titers were significantly lower in elderly participants. Although the increment of antibody levels after the second immunization was higher in elderly participants, the absolute mean titer of this group remained lower than the <60 group. After the second vaccination, 31.3 % of the elderly had no detectable neutralizing antibodies in contrast to the younger group, in which only 2.2% had no detectable neutralizing antibodies.

Conclusion: Our data showed differences between the antibody responses raised after the first and second BNT162b2 vaccination, in particular lower frequencies of neutralizing antibodies in the elderly group. This suggests that this population needs to be closely monitored and may require earlier revaccination or/and an increased vaccine dose to ensure stronger long lasting immunity and protection against infection."

Lancet Infect Dis: [Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study](#) (27 April 2021)

"In this large prospective observational study, we assessed adverse effects from the two COVID-19 vaccines in use in the UK at the time of writing (BNT162b2 and ChAdOx1 nCoV-19), as well as self-reported infection rates following one dose or two doses of BNT162b2 and one dose of ChAdOx1 nCoV-19. Reported side-effects were minor in severity and of short duration. Headache and fatigue were more common in women than in men, in people aged 55 years or younger than in people older than 55 years, and after the second than after the first dose. Individuals with known past SARS-CoV-2 infection were more likely to have adverse effects after the first dose than were those without known past infection. We found, in a community setting, that self-reported infection rates of those vaccinated with the BNT162b2 or ChAdOx1 nCoV-19 vaccines were significantly lower than infection rates in

unvaccinated controls. Documented infection rates in our app after a single vaccine dose decreased by 58% (95% CI 54–62) at 12–20 days, 69% (66–72) at 21–44 days, and 72% (63–79) after 45–59 days following BNT162b2, and 39% (21–53) at 12–20 days and 60% (49–68) at 21–44 days following ChAdOx1 nCoV-19, compared with unvaccinated controls.

Localised and systemic side-effects after vaccination are less common in a real-world community setting than reported in phase 3 trials, mostly minor in severity, and self-limiting. Our data will enable prediction of side-effects based on age, sex, and past COVID-19 status to help update guidance to health professionals to reassure the population about the safety of vaccines."

MMWR: [Updated Recommendations from the Advisory Committee on Immunization Practices for Use of the Janssen \(Johnson & Johnson\) COVID-19 Vaccine After Reports of Thrombosis with Thrombocytopenia Syndrome Among Vaccine Recipients — United States, April 2021](#) (27 April 2021)

"What is already known about this topic? On April 13, 2021, CDC and the Food and Drug Administration (FDA) recommended pausing use of the Janssen COVID-19 vaccine after reports of thrombosis with thrombocytopenia syndrome (TTS) among vaccine recipients.

What is added by this report? On April 23, the Advisory Committee on Immunization Practices concluded that the benefits of resuming Janssen COVID-19 vaccination among persons aged ≥18 years outweighed the risks and reaffirmed its interim recommendation under FDA's Emergency Use Authorization, which includes a new warning for rare clotting events among women aged 18–49 years.

What are the implications for public health practice? Resuming use of the Janssen COVID-19 vaccine will ensure flexibility, choice, and improved access. Education about TTS risk with Janssen COVID-19 vaccine is critical."

Clin Infect Dis: [Effectiveness of mRNA COVID-19 vaccines against SARS-CoV-2 infection in a cohort of healthcare personnel](#) (26 April 2021)

"In a large cohort of US healthcare personnel (HCP) without prior COVID-19 infection, 94,382 doses of mRNA COVID-19 vaccine were administered to 49,220 individuals. The adjusted vaccine effectiveness following two doses of each of the two available brands of mRNA vaccine exceeded 96%."

Gut: [Infliximab is associated with attenuated immunogenicity to BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines in patients with IBD](#) (26 April 2021)

"Objective: Delayed second dose SARS-CoV-2 vaccination trades maximal effectiveness for a lower level of immunity across more of the population. We investigated whether patients

with inflammatory bowel disease treated with infliximab have attenuated serological responses to a single dose of a SARS-CoV-2 vaccine.

Design: Antibody responses and seroconversion rates in infliximab-treated patients (n=865) were compared with a cohort treated with vedolizumab (n=428), a gut-selective anti-integrin $\alpha 4\beta 7$ monoclonal antibody. Our primary outcome was anti-SARS-CoV-2 spike (S) antibody concentrations, measured using the Elecsys anti-SARS-CoV-2 spike (S) antibody assay 3-10 weeks after vaccination, in patients without evidence of prior infection. Secondary outcomes were seroconversion rates (defined by a cut-off of 15 U/mL), and antibody responses following past infection or a second dose of the BNT162b2 vaccine.

Results: Geometric mean (SD) anti-SARS-CoV-2 antibody concentrations were lower in patients treated with infliximab than vedolizumab, following BNT162b2 (6.0 U/mL (5.9) vs 28.8 U/mL (5.4) $p < 0.0001$) and ChAdOx1 nCoV-19 (4.7 U/mL (4.9)) vs 13.8 U/mL (5.9) $p < 0.0001$) vaccines. In our multivariable models, antibody concentrations were lower in infliximab-treated compared with vedolizumab-treated patients who received the BNT162b2 (fold change (FC) 0.29 (95% CI 0.21 to 0.40), $p < 0.0001$) and ChAdOx1 nCoV-19 (FC 0.39 (95% CI 0.30 to 0.51), $p < 0.0001$) vaccines. In both models, age ≥ 60 years, immunomodulator use, Crohn's disease and smoking were associated with lower, while non-white ethnicity was associated with higher, anti-SARS-CoV-2 antibody concentrations. Seroconversion rates after a single dose of either vaccine were higher in patients with prior SARS-CoV-2 infection and after two doses of BNT162b2 vaccine.

Conclusion: Infliximab is associated with attenuated immunogenicity to a single dose of the BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines. Vaccination after SARS-CoV-2 infection, or a second dose of vaccine, led to seroconversion in most patients. Delayed second dosing should be avoided in patients treated with infliximab."

Clin Infect Dis: [First dose of BNT162b2 mRNA vaccine in a Health Care Worker cohort is associated with reduced symptomatic and asymptomatic SARS-CoV-2 infection](#) (24 April 2021)

"Over the first 2 months of 2021 vaccination coverage of staff at Hull Teaching Hospitals with BNT162b2 increased from 8.3% to 82.5%, and was associated with a significant reduction in symptomatic and asymptomatic SARS-CoV-2 cases. The proportion of positive lateral flow tests from asymptomatic screening was maintained over this period."

Treatments and Management

News in Brief

An antiviral pill to treat COVID-19 could be ready by the end of the year, according to Pfizer ([Forbes](#)).

Peer-Reviewed Articles

Ann Intern Med: [The Reign of the Ventilator: Acute Respiratory Distress Syndrome, COVID-19, and Technological Imperatives in Intensive Care](#) (04 May 2021)

Some history of medicine:

"In the early phase of the COVID-19 pandemic, a dispute arose as to whether the disease caused a typical or atypical version of acute respiratory distress syndrome (ARDS). This essay recounts the emergence of ARDS and places it in the context of the technological transformation of modern hospital care-particularly the emergence of intensive care after the 1952 Copenhagen polio epidemic. The polio epidemic seemed to show the value of manual positive-pressure ventilation, leading to the proliferation of mechanical ventilators and the expansion of intensive care units in the 1960s. This created the conditions of possibility for ARDS to be described and institutionalized within modern intensive care. Yet the centrality of the ventilator to descriptions and definitions of ARDS quickly made it difficult to conceive of the disorder outside the framework of mechanical ventilation and blood gas levels, or to acknowledge the degree to which the ventilator was a source of iatrogenic injury and complications. Moreover, the imperative to understand and treat ARDS with mechanical ventilation set the stage for the early confusion about whether patients with COVID-19 should receive mechanical ventilation. This history offers many crucial lessons about how new technologies can lead to new and valuable therapies but can also subtly shape and constrain medical thinking. Moreover, ventilators not only changed how respiratory disorders were conceived; they also brought new forms of respiratory illness into existence."

Lancet: [Tocilizumab in patients admitted to hospital with COVID-19 \(RECOVERY\): a randomised, controlled, open-label, platform trial](#) (01 May 2021)

"This randomised, controlled, open-label, platform trial (Randomised Evaluation of COVID-19 Therapy [RECOVERY]), is assessing several possible treatments in patients hospitalised with COVID-19 in the UK. Those trial participants with hypoxia (oxygen saturation <92% on air or requiring oxygen therapy) and evidence of systemic inflammation (C-reactive protein ≥ 75 mg/L) were eligible for random assignment in a 1:1 ratio to usual standard of care alone versus usual standard of care plus tocilizumab at a dose of 400 mg–800 mg (depending on weight) given intravenously. A second dose could be given 12–24 h later if the patient's condition had not improved. The primary outcome was 28-day mortality, assessed in the intention-to-treat population. The trial is registered with ISRCTN (50189673) and ClinicalTrials.gov (NCT04381936).

Between April 23, 2020, and Jan 24, 2021, 4116 adults of 21 550 patients enrolled into the RECOVERY trial were included in the assessment of tocilizumab, including 3385 (82%) patients receiving systemic corticosteroids. Overall, 621 (31%) of the 2022 patients

allocated tocilizumab and 729 (35%) of the 2094 patients allocated to usual care died within 28 days (rate ratio 0.85; 95% CI 0.76–0.94; $p=0.0028$). Consistent results were seen in all prespecified subgroups of patients, including those receiving systemic corticosteroids. Patients allocated to tocilizumab were more likely to be discharged from hospital within 28 days (57% vs 50%; rate ratio 1.22; 1.12–1.33; $p<0.0001$). Among those not receiving invasive mechanical ventilation at baseline, patients allocated tocilizumab were less likely to reach the composite endpoint of invasive mechanical ventilation or death (35% vs 42%; risk ratio 0.84; 95% CI 0.77–0.92; $p<0.0001$).

In hospitalised COVID-19 patients with hypoxia and systemic inflammation, tocilizumab improved survival and other clinical outcomes. These benefits were seen regardless of the amount of respiratory support and were additional to the benefits of systemic corticosteroids."

J Antimicrob Chemother: [In vitro antiviral activity of the anti-HCV drugs daclatasvir and sofosbuvir against SARS-CoV-2, the aetiological agent of COVID-19](#) (21 April 2021)

"Current approaches of drug repurposing against COVID-19 have not proven overwhelmingly successful and the SARS-CoV-2 pandemic continues to cause major global mortality. SARS-CoV-2 nsp12, its RNA polymerase, shares homology in the nucleotide uptake channel with the HCV orthologue enzyme NS5B. Besides, HCV enzyme NS5A has pleiotropic activities, such as RNA binding, that are shared with various SARS-CoV-2 proteins. Thus, anti-HCV NS5B and NS5A inhibitors, like sofosbuvir and daclatasvir, respectively, could be endowed with anti-SARS-CoV-2 activity.

SARS-CoV-2-infected Vero cells, HuH-7 cells, Calu-3 cells, neural stem cells and monocytes were used to investigate the effects of daclatasvir and sofosbuvir. In silico and cell-free based assays were performed with SARS-CoV-2 RNA and nsp12 to better comprehend the mechanism of inhibition of the investigated compounds. A physiologically based pharmacokinetic model was generated to estimate daclatasvir's dose and schedule to maximize the probability of success for COVID-19.

Daclatasvir inhibited SARS-CoV-2 replication in Vero, HuH-7 and Calu-3 cells, with potencies of 0.8, 0.6 and 1.1 μM , respectively. Although less potent than daclatasvir, sofosbuvir alone and combined with daclatasvir inhibited replication in Calu-3 cells. Sofosbuvir and daclatasvir prevented virus-induced neuronal apoptosis and release of cytokine storm-related inflammatory mediators, respectively. Sofosbuvir inhibited RNA synthesis by chain termination and daclatasvir targeted the folding of secondary RNA structures in the SARS-CoV-2 genome. Concentrations required for partial daclatasvir in vitro activity are achieved in plasma at C_{max} after administration of the approved dose to humans.

Daclatasvir, alone or in combination with sofosbuvir, at higher doses than used against HCV, may be further fostered as an anti-COVID-19 therapy."

Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases

News in Brief

"COVID 'doesn't discriminate by age': Serious cases on the rise in younger adults" ([NPR](#)).

Long read: "A crisis of undiagnosed cancers is emerging in the pandemic's second year" ([ProPublica](#)).

Peer-Reviewed Articles

Open Forum Infect Dis: [Characterization of Bacterial and Fungal Infections in Hospitalized Patients with COVID-19 and Factors Associated with Healthcare-associated Infections](#) (05 May 2021)

"Patients hospitalized with COVID-19 are at increased risk of healthcare-associated infections especially with prolonged hospital stays. We sought to identify incidence, antimicrobial susceptibilities, and outcomes associated with bacterial/fungal secondary infections in a large cohort of patients with COVID-19.

We evaluated adult patients diagnosed with COVID-19 between March 2 to May 31, 2020 and hospitalized >24 hours. Data extracted from medical records included diagnoses, vital signs, laboratory results, microbiological data, and antibiotic use. Microbiologically-confirmed bacterial and fungal pathogens from clinical cultures were evaluated to characterize community- and healthcare-associated infections, including describing temporal changes in predominant organisms on presentation and throughout hospitalization. Univariable and multivariable logistic regression analyses were performed to investigate risk factors for healthcare-associated infections.

A total of 3,028 patients were included and accounted for 899 positive clinical cultures. Overall, 516 (17%) with positive cultures met criteria for infection. Community-associated co-infections were identified in 183 (6%) patients, whereas healthcare-associated infections occurred in 350 (12%) patients. 57% of healthcare-associated infections were caused by Gram-negative bacteria and 19% by fungi. Antibiotic resistance increased with longer hospital stays, with incremental increases in the proportion of vancomycin-resistance among enterococci and ceftriaxone- and carbapenem-resistance among Enterobacterales. ICU stay, invasive mechanical ventilation, and steroids were associated with healthcare-associated infections.

Healthcare-associated infections occur in a small proportion of patients hospitalized with COVID-19 and are most often caused by Gram-negative and fungal pathogens. Antibiotic resistance is more prevalent with prolonged hospital stays. Antimicrobial stewardship is imperative in this population to minimize unnecessary broad-spectrum antibiotics."

Diabetologica: [Risk phenotypes of diabetes and association with COVID-19 severity and death: a living systematic review and meta-analysis](#) (28 April 2021)

"Methods: This is the first edition of a living systematic review and meta-analysis on observational studies investigating phenotypes in individuals with diabetes and COVID-19-related death and severity. Four different databases were searched up to 10 October 2020. We used a random effects meta-analysis to calculate summary relative risks (SRR) with 95% CI. The certainty of evidence was evaluated by the GRADE tool.

Results: A total of 22 articles, including 17,687 individuals, met our inclusion criteria. For COVID-19-related death among individuals with diabetes and COVID-19, there was high to moderate certainty of evidence for associations (SRR [95% CI]) between male sex (1.28 [1.02, 1.61], n = 10 studies), older age (>65 years: 3.49 [1.82, 6.69], n = 6 studies), pre-existing comorbidities (cardiovascular disease: 1.56 [1.09, 2.24], n = 8 studies; chronic kidney disease: 1.93 [1.28, 2.90], n = 6 studies; chronic obstructive pulmonary disease: 1.40 [1.21, 1.62], n = 5 studies), diabetes treatment (insulin use: 1.75 [1.01, 3.03], n = 5 studies; metformin use: 0.50 [0.28, 0.90], n = 4 studies) and blood glucose at admission (≥ 11 mmol/l: 8.60 [2.25, 32.83], n = 2 studies). Similar, but generally weaker and less precise associations were observed between risk phenotypes of diabetes and severity of COVID-19.

Conclusions/interpretation: Individuals with a more severe course of diabetes have a poorer prognosis of COVID-19 compared with individuals with a milder course of disease. To further strengthen the evidence, more studies on this topic that account for potential confounders are warranted."

Lancet Diabetes Endocrinol: [Associations between body-mass index and COVID-19 severity in 6.9 million people in England: a prospective, community-based, cohort study](#) (28 April 2021)

"In this very large, community-based cohort study, we found that the hazard ratio of severe outcomes from COVID-19 (ie, admission to hospital, admission to ICU, or death) increase progressively above a BMI of 23 kg/m², which is not attributable to excess risks of related diseases such as type 2 diabetes. We found that BMI is a greater risk factor for younger people (aged 20–39 years) than for older people (≥ 80 years), and for Black people than for White people.

Even a small increase in BMI above 23 kg/m² is a risk factor for adverse outcomes after infection with SARS-CoV-2. People with excess weight, even without other comorbidities, are at substantially increased risk of admission to hospital and ICU and death due to COVID-19, especially for younger adults and Black people. Excess weight is a modifiable risk factor and investment in the treatment of overweight and obesity and long-term preventive strategies could help reduce the severity of COVID-19 disease."

Long COVID / Post-COVID Period

News in Brief

"An inside look at a post–COVID-19 clinic" ([JAMA](#)).

Long read: "Scientists set out to connect the dots on long COVID" ([Nat Methods](#)).

Peer-Reviewed Articles

Lancet Respir Med: [3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a prospective study](#) (05 May 2021)

"The consequences of COVID-19 in those who recover from acute infection requiring hospitalisation have yet to be clearly defined. We aimed to describe the temporal trends in respiratory outcomes over 12 months in patients hospitalised for severe COVID-19 and to investigate the associated risk factors.

In this prospective, longitudinal, cohort study, patients admitted to hospital for severe COVID-19 who did not require mechanical ventilation were prospectively followed up at 3 months, 6 months, 9 months, and 12 months after discharge from Renmin Hospital of Wuhan University, Wuhan, China. Patients with a history of hypertension; diabetes; cardiovascular disease; cancer; and chronic lung disease, including asthma or chronic obstructive pulmonary disease; or a history of smoking documented at time of hospital admission were excluded at time of electronic case-note review. Patients who required intubation and mechanical ventilation were excluded given the potential for the consequences of mechanical ventilation itself to influence the factors under investigation. During the follow-up visits, patients were interviewed and underwent physical examination, routine blood test, pulmonary function tests (ie, diffusing capacity of the lungs for carbon monoxide [DLCO]; forced expiratory flow between 25% and 75% of forced vital capacity [FVC]; functional residual capacity; FVC; FEV1; residual volume; total lung capacity; and vital capacity), chest high-resolution CT (HRCT), and 6-min walk distance test, as well as assessment using a modified Medical Research Council dyspnoea scale (mMRC).

Between Feb 1, and March 31, 2020, of 135 eligible patients, 83 (61%) patients participated in this study. The median age of participants was 60 years (IQR 52–66). Temporal improvement in pulmonary physiology and exercise capacity was observed in most patients; however, persistent physiological and radiographic abnormalities remained in some patients with COVID-19 at 12 months after discharge. We found a significant reduction in DLCO over the study period, with a median of 77% of predicted (IQR 67–87) at 3 months, 76% of predicted (68–90) at 6 months, and 88% of predicted (78–101) at 12 months after discharge. At 12 months after discharge, radiological changes persisted in 20 (24%) patients.

Multivariate logistic regression showed increasing odds of impaired DLCO associated with female sex (odds ratio 8.61 [95% CI 2.83–26.2; $p=0.0002$]) and radiological abnormalities were associated with peak HRCT pneumonia scores during hospitalisation (1.36 [1.13–1.62]; $p=0.0009$).

In most patients who recovered from severe COVID-19, dyspnoea scores and exercise capacity improved over time; however, in a subgroup of patients at 12 months we found evidence of persistent physiological and radiographic change. A unified pathway for the respiratory follow-up of patients with COVID-19 is required."

Clin Infect Dis: [Development and validation of the long covid symptom and impact tools, a set of patient-reported instruments constructed from patients' lived experience](#) (29 April 2021)

"The long covid Symptom and Impact Tools (ST and IT) were constructed from the answers to a survey with open-ended questions to 492 patients with long COVID. Validation of the tools involved adult patients with suspected or confirmed COVID-19 and symptoms extending over three weeks after onset. Construct validity was assessed by examining the relations of the ST and IT scores with health related quality of life (EQ-5D-5L), function (PCFS, post-COVID functional scale), and perceived health (MYMOP2). Reliability was determined by a test-retest. The "patient acceptable symptomatic state" (PASS) was determined by the percentile method.

Validation involved 1022 participants (55% with confirmed COVID-19, 79% female, and 12.5% hospitalized for COVID-19). The long COVID ST and IT scores were strongly correlated with the EQ-5D-5L ($r_s = -0.45$ and $r_s = -0.59$ respectively), the PCFS ($r_s = -0.39$ and $r_s = -0.55$), and the MYMOP2 ($r_s = -0.40$ and $r_s = -0.59$). Reproducibility was excellent with an interclass correlation coefficient of 0.83 (95% confidence interval 0.80 to 0.86) for the ST score and 0.84 (0.80 to 0.87) for the IT score. In total, 793 (77.5%) patients reported an unacceptable symptomatic state, thereby setting the PASS for the long covid IT score at 30 (28 to 33).

The long covid ST and IT tools, constructed from patients' lived experiences, provide the first validated and reliable instruments for monitoring the symptoms and impact of long covid."

J Intern Med: [Half-year follow-up of patients recovering from severe COVID-19: Analysis of symptoms and their risk factors](#) (27 April 2021)

"We followed up 1174 patients with severe coronavirus disease 2019 (COVID-19) who were recovered and discharged for 6 months.

There were 175 cases with clear IgG results 6 months after discharge, of which 82 (46.9%) were IgG (+) and 16 (9.1%) were IgG (dim+). Four hundred and forty-one participants (55.4%) had some kind of sequelae. The most common symptoms were fatigue (25.3%),

sleep disorder (23.2%) and shortness of breath (20.4%). In those who had sequelae, 262 (59.4%) had more than one symptom. Critical cases were more likely to have cough (20.5% vs 11.6%, $p = 0.023$) and hypomnesia (15.1% vs 8.0%, $p = 0.041$) than severe cases. Furthermore, univariate and multivariate logistic regression analyses revealed that women are more likely to have multiple symptoms ($p = 0.002$), fatigue ($p = 0.009$) and sleep disorder ($p = 0.008$), whereas critical illness was found as independent risk factor for hypomnesia ($p = 0.045$).

Our study demonstrated the duration of antibody and sequelae of COVID-19 and compared the differences amongst different populations."

Clin Infect Dis: [Medium-term outcome of severe to critically ill patients with SARS-CoV-2 infection](#) (24 April 2021)

"Background: The medium and long-term effects of severe SARS-CoV-2 infection on survivors are unknown. Here we studied the medium term effects of COVID-19 on survivors of severe disease.

Methods: This is a retrospective, case series of 200 patients hospitalised across three large Birmingham hospitals with severe-to-critical COVID-19 infection 4-7 months from disease-onset. Patients underwent comprehensive clinical, laboratory, imaging, lung function test, quality of life and cognitive assessments.

Results: At 4-7 months from disease-onset, 63.2% of patients experienced persistent breathlessness, 53.5% complained of significant fatigue, 37.5% reduced mobility and 36.8% pain. Serum markers of inflammation and organ injuries that persisted at hospital discharge had normalised on follow-up indicating no sustained immune response causing chronic maladaptive inflammation. Chest radiographs showed a complete resolution in 82.8%; and significantly improved or no change in 17.2%. Lung function test (LFT) revealed gas transfer abnormalities in 80.0% and spirometry in 37.6% patients. Patients with breathlessness had significantly high incidence of comorbidities, abnormal residual chest X-ray and LFT ($p < 0.01$ to all). In all parameters assessed and persisting symptoms there was no statically significant difference between patients managed on hospital wards and on ITU groups. All patients reported a significantly reduced quality of life in all domains of the EQ-5D-5L quality of life measures.

Conclusions and relevance: A significant proportion of COVID-19 with severe illness experience ongoing symptoms of breathlessness, fatigue, pain, reduced mobility, depression and reduced quality of life at 4-7 months from disease-onset. Symptomatic patients tend to have more residual CXR and LFT abnormalities."

JAMA Netw Open: [Acute Ischemic Stroke During the Convalescent Phase of Asymptomatic COVID-2019 Infection in Men](#) (22 April 2021)

"Question Is the risk of acute ischemic stroke (AIS) elevated in patients in the convalescent phase of an asymptomatic COVID-19 infection?

Findings In this case series of 18 male adults aged 50 years or younger who presented with AIS during the convalescent phase of an asymptomatic COVID-19 infection confirmed by a positive SARS-CoV-2 serological (antibodies) test result, the median onset of stroke was 2 months after the diagnosis of COVID-19.

Meaning Results of this study suggest a persistent increased risk of AIS in individuals with asymptomatic COVID-19 months after serological diagnosis, warranting stroke units to be on alert and use SARS-CoV-2 serological testing."

Women's Health, Pregnancy, and Perinatal Care

News in Brief

"Brazil warns women to delay pregnancy amid Covid-19 surge" ([Guardian](#)).

Meanwhile, provisional data suggest that the US birthrate fell by 4% in 2020, another record low ([NPR](#)).

Peer-Reviewed Articles

JAMA: [Association of Maternal SARS-CoV-2 Infection in Pregnancy With Neonatal Outcomes](#) (29 April 2021)

"Question What are the outcomes in newborn infants of mothers testing positive for SARS-CoV-2 in pregnancy?

Findings In this nationwide, prospective cohort study that included 88 159 infants from Sweden, SARS-CoV-2 infection in pregnancy was significantly associated with higher risk of any neonatal respiratory disorder (2.8% vs 2.0%; odds ratio, 1.42) and some other neonatal morbidities, but not neonatal mortality (0.30% vs 0.12%; odds ratio, 2.55).

Meaning Maternal SARS-CoV-2 infection in pregnancy was significantly associated with small increases in the absolute risk of respiratory disorders and some other neonatal morbidities."

JAMA Netw Open: [Association of Maternal Perinatal SARS-CoV-2 Infection With Neonatal Outcomes During the COVID-19 Pandemic in Massachusetts](#) (23 April 2021)

"Question What are the test result positivity rate and health outcomes of maternal SARS-CoV-2 infection among perinatally exposed newborns?

Findings In this cohort study of 255 neonates born to women with positive SARS-CoV-2 test results within 2 weeks before and 72 hours after delivery, 88.2% of newborns were tested for the virus during the birth hospitalization and 2.2% had positive results. A main risk factor for neonatal test result positivity was maternal social vulnerability, and the burden of SARS-CoV-2 exposure on newborn health was associated with preterm delivery, which was prompted by worsening maternal COVID-19 illness.

Meaning Results of this study indicate that neonates who were perinatally exposed to SARS-CoV-2 can sustain adverse health outcomes both directly (as evidenced by higher test result positivity rates when born to socially vulnerable mothers) and indirectly (given the sequelae of preterm birth)."

J Womens Health: [Depression, Anxiety, Resilience, and Coping: The Experience of Pregnant and New Mothers During the First Few Months of the COVID-19 Pandemic](#) (12 April 2021)

"It is well-documented that the mental health of pregnant and postpartum women is essential for maternal, child, and family well-being. Of major public health concern is the perinatal mental health impacts that may occur during the ongoing COVID-19 pandemic.

The purpose of this study is to evaluate the experiences of pregnant and postpartum women (n = 524) in the United States in the early phase of the COVID-19 pandemic. This cross-sectional online observational study collected psychosocial quantitative and qualitative survey data in adult pregnant and postpartum (up to 6 months postdelivery) women in April–June 2020.

Multivariable linear regression models were used to evaluate predictors of depressive symptoms, anxiety, and post-traumatic stress disorder. The most common predictors were job insecurity, family concerns, eating comfort foods, resilience/adaptability score, sleep, and use of social and news media. Qualitative themes centered on pervasive uncertainty and anxiety; grief about losses; gratitude for shifting priorities; and use of self-care methods including changing media use.

This study provides information to identify risk for anxiety, depression, and PTSD symptoms in perinatal women during acute public health situations. Women with family and job concerns and low resilience/adaptability scores seem to be at high risk of psychological sequelae. Although use of social media is thought to improve social connectedness, our results indicate that increased media consumption is related to increased anxiety symptoms."

Pediatric Population

News in Brief

"Children now account for 22% of new U.S. COVID cases. Why is that?" ([NPR](#)).

"Here's what the CDC says summer camps should do to prevent and respond to COVID cases" ([NPR](#); see also: [updated CDC guidance](#)).

Long read: "The lost year: What the pandemic cost teenagers" ([ProPublica](#)).

Vaccines

The FDA could authorize the Pfizer/BioNTech COVID-19 vaccine for adolescents 12-15 as early next week ([NYT](#)).

Pfizer is planning on seeking FDA authorization for its vaccine for kids 2-11 by this fall ([CNN](#)), with results from trials in infants expected around that time ([Reuters](#)).

Podcast: "Kids and COVID vaccines" ([Nature](#)).

Peer-Reviewed Articles

JAMA Netw Open: [Clinical Characteristics and Transmission of COVID-19 in Children and Youths During 3 Waves of Outbreaks in Hong Kong](#) (03 May 2021)

"Question What were the major sources of infection among children and youths with COVID-19 in Hong Kong in 2020?

Findings In this cross-sectional study of 397 children and youths with COVID-19 in the first 3 waves of outbreaks in Hong Kong, in 2020, the largest group had no recent international travel, and nearly all individuals were reported to have other family members with COVID-19. Three students studying in the same school contracted COVID-19, and few children or youths with no recent international travel reported unknown contact histories.

Meaning These findings suggest that households and not schools were the major route of transmission among children and youths with COVID-19 in Hong Kong."

Pediatrics: [Socioeconomic and Racial and/or Ethnic Disparities in Multisystem Inflammatory Syndrome](#) (01 May 2021; published online 18 February 2021)

"OBJECTIVES: To characterize the socioeconomic and racial and/or ethnic disparities impacting the diagnosis and outcomes of multisystem inflammatory syndrome in children (MIS-C).

METHODS: This multicenter retrospective case-control study was conducted at 3 academic centers from January 1 to September 1, 2020. Children with MIS-C were compared with 5 control groups: children with coronavirus disease 2019, children evaluated for MIS-C who did not meet case patient criteria, children hospitalized with febrile illness, children with Kawasaki disease, and children in Massachusetts based on US census data. Neighborhood socioeconomic status (SES) and social vulnerability index (SVI) were measured via a census-based scoring system. Multivariable logistic regression was used to examine associations between SES, SVI, race and ethnicity, and MIS-C diagnosis and clinical severity as outcomes.

RESULTS: Among 43 patients with MIS-C, 19 (44%) were Hispanic, 11 (26%) were Black, and 12 (28%) were white; 22 (51%) were in the lowest quartile SES, and 23 (53%) were in the highest quartile SVI. SES and SVI were similar between patients with MIS-C and coronavirus disease 2019. In multivariable analysis, lowest SES quartile (odds ratio 2.2 [95% confidence interval 1.1–4.4]), highest SVI quartile (odds ratio 2.8 [95% confidence interval 1.5–5.1]), and racial and/or ethnic minority background were associated with MIS-C diagnosis. Neither SES, SVI, race, nor ethnicity were associated with disease severity.

CONCLUSIONS: Lower SES or higher SVI, Hispanic ethnicity, and Black race independently increased risk for MIS-C. Additional studies are required to target interventions to improve health equity for children."

Pediatrics: [Remestemcel-L Therapy for COVID-19–Associated Multisystem Inflammatory Syndrome in Children](#) (01 May 2021; published online 12 February 2021)

"Multisystem inflammatory syndrome in children (MIS-C) is a serious postinfectious immune dysregulation associated with coronavirus disease 2019 that may present with severe and life-threatening cardiovascular dysfunction, hemodynamic instability, shock, and multisystem organ failure. Optimal treatment is unknown. Current standard of care consists of nonspecific anti-inflammatory and antithrombotic therapies. Interventions that target MIS-C's distinctive clinical features and immunophenotype are indicated. Remestemcel-L, an investigational mesenchymal stromal cell therapy, is a promising candidate for treatment of MIS-C because of its beneficial anti-inflammatory, immunomodulatory, endothelial function and vascular stabilizing effects, which align well with the pathophysiology of MIS-C. Here, we present the first two patients with life-threatening MIS-C ever treated with remestemcel-L under an expanded access program. Both were previously healthy children without any indication of previous coronavirus disease 2019 infection or exposure. They presented with severe clinical illness including myocardial dysfunction, hemodynamic instability, hypotension, acute kidney injury, and shock. At the time of hospital admission, both had negative polymerase chain reaction (PCR) test results and positive serology results for severe acute respiratory syndrome coronavirus 2. Both children received standard of care MIS-C treatment. Although the patients showed some clinical improvement, left ventricular ejection fraction remained reduced and inflammatory biomarkers remained

significantly elevated. When treated with two intravenous doses of remestemcel-L separated by 48 hours, rapid normalization of left ventricular ejection fraction, notable reductions in biomarkers of systemic and cardiac inflammation, and improved clinical status occurred. Neither child experienced adverse effects associated with remestemcel-L administration. This treatment appears promising as a novel immunomodulatory cellular therapy for children with clinically significant cardiovascular manifestations of MIS-C."

JAMA Netw Open: [Caregiver Perceptions of Children's Psychological Well-being During the COVID-19 Pandemic](#) (29 April 2021)

"Question Is the COVID-19 pandemic and stressor exposure associated with caregivers' perceptions of children's psychological well-being?

Findings In this survey study among 32 217 caregivers of public-school students, endorsement of child mental health concerns was significantly higher and endorsement of positive adjustment characteristics was significantly lower after the end of in-person instruction compared with before. After accounting for covariates, child mental health concerns increased in probability and positive adjustment characteristics decreased in probability as COVID-19 exposure and family stressors increased.

Meaning These findings suggest that COVID-19 was associated with negative caregiver perceptions of children's psychological well-being, requiring a comprehensive public health strategy."

Science: [Household COVID-19 risk and in-person schooling](#) (29 April 2021)

"In-person schooling has proved contentious and difficult to study throughout the SARS-CoV-2 pandemic. Data from a massive online survey in the United States indicates an increased risk of COVID-19-related outcomes among respondents living with a child attending school in-person. School-based mitigation measures are associated with significant reductions in risk, particularly daily symptoms screens, teacher masking, and closure of extra-curricular activities. A positive association between in-person schooling and COVID-19 outcomes persists at low levels of mitigation, but when seven or more mitigation measures are reported, a significant relationship is no longer observed. Among teachers, working outside the home was associated with an increase in COVID-19-related outcomes, but this association is similar to other occupations (e.g., healthcare, office work). While in-person schooling is associated with household COVID-19 risk, this risk can likely be controlled with properly implemented school-based mitigation measures."

JAMA: [Reasons for Admissions to US Children's Hospitals During the COVID-19 Pandemic](#) (27 April 2021)

"This study uses Pediatric Health Information System database data to compare hospitalizations in US children's hospitals early in the COVID-19 pandemic (March-August

2020) vs the same period in 2017-2019, overall and for respiratory, chronic, nonrespiratory, and other conditions."

Diabetes Care: [Spike in Diabetic Ketoacidosis Rates in Pediatric Type 2 Diabetes During the COVID-19 Pandemic](#) (26 April 2021)

"BACKGROUND The impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) on the incidence of new-onset type 2 diabetes and diabetic ketoacidosis (DKA) is unclear. It is unknown whether the coincidence of DKA noted in adult patients with type 2 diabetes is an issue for youth during the coronavirus disease 2019 pandemic.

RESEARCH DESIGN AND METHODS A retrospective single-center medical record review was conducted in a large, urban children's hospital of pediatric subjects presenting with new-onset type 2 diabetes between March and August of 2018 to 2020.

RESULTS The proportion of subjects presenting with new-onset type 2 diabetes in DKA dramatically increased in 2020 (9% in 2018, 3% in 2019, and 20% in 2020, $P = 0.029$).

CONCLUSIONS In 2020, youth with new-onset type 2 diabetes had a greater incidence of DKA at presentation than previously observed. Future studies should examine the impact of SARS-CoV2 exposure on the presentation of type 2 diabetes in all age groups to inform better patient care."

Pediatrics: [Hospital Admissions for Abusive Head Trauma at Children's Hospitals During COVID-19](#) (20 April 2021)

"We hypothesized that in the case of potentially life-threatening abuse, such as abusive head trauma (AHT), it is more difficult for caregivers to forgo medical care....

The Pediatric Health Information System (PHIS), a database of 51 children's hospitals in the United States (U.S.), was used to identify hospitalizations for AHT from 1/1/17 to 9/30/20 in children < 5 years of age. This study was limited to 49 hospitals with consistent contributions to the PHIS since 2017....

Of the 1,216,336 hospitalizations for children < age 5, 1317 (0.1%) were for AHT. Of these, 750 occurred between March 11 and September 30, 127 (16%) of which were in 2020. Compared to 2017-2019, children hospitalized with AHT during 2020 had a shorter length of stay but were otherwise similar regarding the percentage of ICU stay, ventilator utilization, subdural hemorrhage, retinal hemorrhage, and mortality....

This study demonstrates a significant decrease in AHT admissions in children < 5 years of age across 49 children's hospitals within the U.S. during the COVID-19 pandemic. The expectation was that child maltreatment would increase due to the emotional and economic stressors of the pandemic."

Mental Health and Wellness

News in Brief

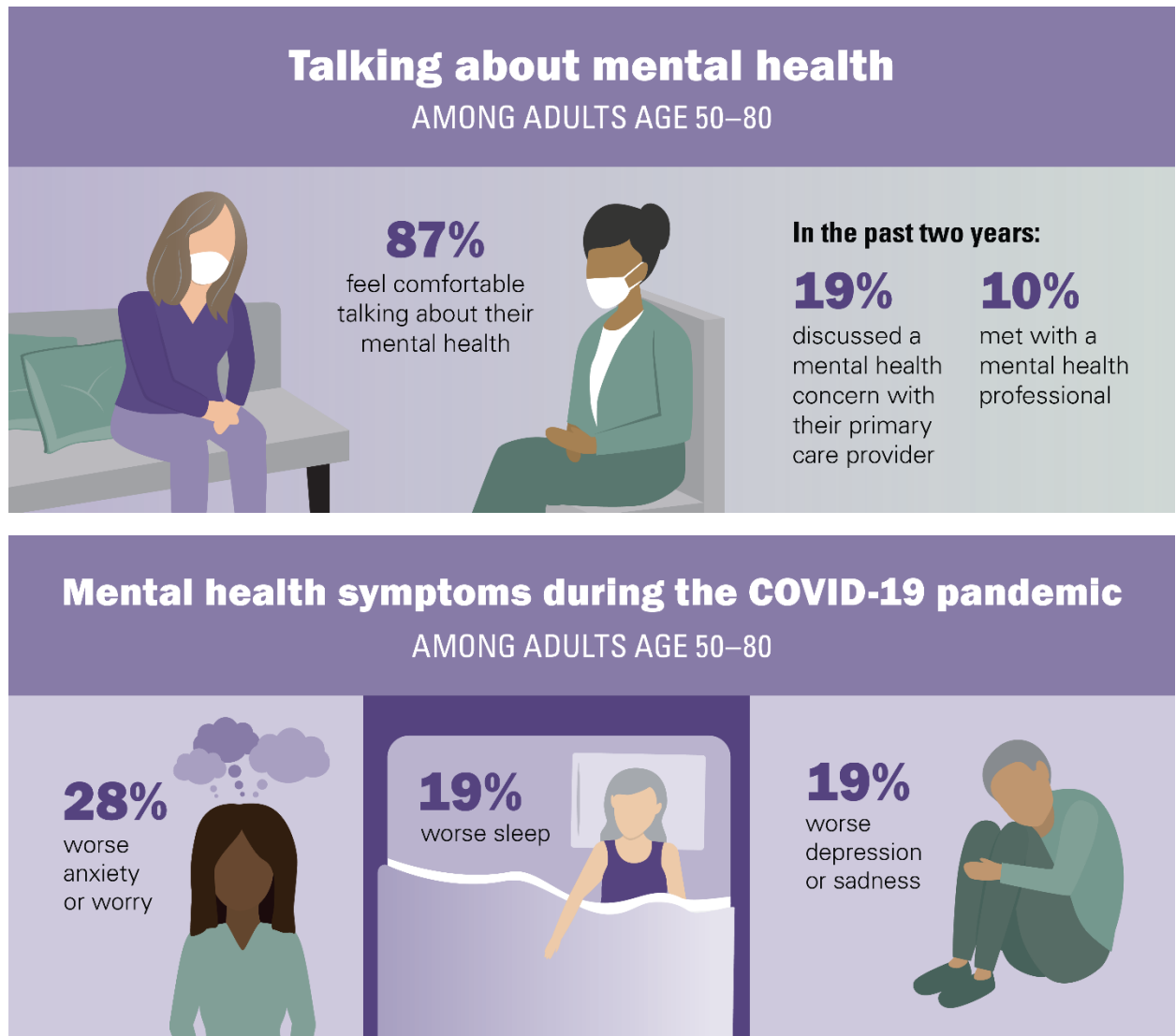
COMIC: "How I cope with pandemic numbness" ([NPR](#)).



Special Reports and Other Resources

UM: [Mental Health Among Older Adults Before and During the COVID-19 Pandemic](#) (04 May 2021)

"An estimated one in five older adults currently experience depression, anxiety, insomnia, substance use, or another mental health disorder. These conditions are not a normal part of aging and can impair physical and social functioning. Identifying and treating them can improve quality of life and overall well-being. The COVID-19 pandemic has created unprecedented challenges for older adults that can negatively affect mental health. In January 2021, the University of Michigan National Poll on Healthy Aging asked a national sample of U.S. adults age 50–80 about their mental health and the effect of the COVID-19 pandemic on their mental health symptoms."



Ed: This is not COVID-related, but included because of perceived importance.

GAO: [Defense Health Care: DOD Needs to Fully Assess Its Non-clinical Suicide Prevention Efforts and Address Any Impediments to Effectiveness](#) (26 April 2021)

"To help address the growing rate of military suicides, DOD provides clinical treatment such as medication to servicemembers. DOD has also implemented various non-clinical suicide prevention efforts, such as distributing gun locks and providing suicide awareness training.

How are these non-clinical interventions working? In short, DOD assesses its entire suicide prevention program, but hasn't assessed all of the efforts individually. Each one should be assessed for effectiveness and to identify potential improvements.

We recommended developing a process to ensure that individual non-clinical suicide prevention efforts are assessed."

Disparities and Health Equity

News in Brief

The NIH is investing \$29 million to address COVID-19 disparities ([NIH](#)).

Long read: "Inequality's deadly toll: A century of research has demonstrated how poverty and discrimination drive disease. Can COVID push science to finally address the issue?" ([Nature](#); see also: [podcast with author](#))

Special Reports and Other Resources

KFF: [Global COVID-19 Vaccine Equity: U.S. Policy Options and Actions to Date](#) (30 April 2021)

"The U.S. is expected to soon have enough COVID-19 vaccine doses on hand to fully vaccinate just about everyone in the country once, and, with additional doses already purchased, could likely vaccinate the population twice over. The same cannot be said for the majority of countries around the world, especially low- and middle-income countries (LMICs) where access has been limited and will remain so for some time. Furthermore, while manufacturers are scaling up vaccine production, total projected production in 2021 of 9.8 billion is still short of estimated need of up to 11.5 billion to vaccinate everyone globally. Recent actions restricting or pausing the use of the AstraZeneca and Johnson & Johnson vaccines in some countries due to extremely rare but serious side effects could reverberate globally, potentially prolonging the vaccine access gap given that these two vaccines have been positioned as key workhorses for ramping up vaccinations in LMICs in particular. Further, the expected need for booster doses and reformulated vaccines to

address waning immunity and variants means global demand is likely to remain extremely high for the foreseeable future. Ultimately, ensuring widespread global access to COVID-19 vaccines, which is key to preventing cases and deaths and contributing to global population immunity, is a significant challenge and one that could threaten the ability to control the pandemic."

Peer-Reviewed Articles

Lancet: [Ethnic differences in SARS-CoV-2 infection and COVID-19-related hospitalisation, intensive care unit admission, and death in 17 million adults in England: an observational cohort study using the OpenSAFELY platform](#) (30 April 2021)

"This is the largest study in the UK to examine ethnic inequalities in testing positive for SARS-CoV-2 and in COVID-19-related outcomes in a cohort covering 40% of the population in England. Additionally, it is the only population-representative study to date that accounts for household size in addition to sociodemographic characteristics and clinical comorbidities. By examining ethnicity according to both high-level and detailed ethnic groupings, we have shown important ethnic differences in the risk of testing positive for SARS-CoV-2 and the risks of COVID-19-related hospital admission, intensive care unit admissions, and death. We showed that multiple factors contribute to ethnic inequalities in COVID-19 and the importance of these factors varies by ethnic group. Compared with wave 1, the risks of COVID-19-related hospitalisation and death in wave 2 were increased for South Asian groups and reduced in all other ethnic minority groups relative to the White group.

The risks of SARS-CoV-2 infection and severe COVID-19 outcomes are disproportionately increased in minority ethnic groups, both in the UK and internationally. Reducing ethnic inequalities in COVID-19 risks requires action on social determinants including addressing disadvantage and discrimination, reducing risk of infection and transmission, improving quality of and access to quality clinical care, and improving management of pre-existing clinical conditions. The appropriate balance of these actions needs tailoring for different ethnic groups."

Risk, Transmission, and Exposure

News in Brief

"The future of coronavirus testing is in Greenville, N.C.: 1 million testing kits, 40,000 families and an ambitious bid to stop community transmission of the virus" ([WP](#)).

"Alaska Airlines bans state lawmaker for her 'continued refusal to comply' with mask mandate" ([CNN](#)).

Peer-Reviewed Articles

Clin Infect Dis: [Widespread SARS-CoV-2 Transmission Among Attendees at a Large Motorcycle Rally and their Contacts, 30 US Jurisdictions, August–September, 2020](#) (29 April 2021)

"The 2020 Sturgis Motorcycle rally resulted in widespread transmission of SARS-CoV-2 across the United States. At least 649 COVID-19 cases were identified, including secondary and tertiary spread to close contacts. To limit transmission, persons attending events should wear masks and practice physical distancing. Persons with a known exposure should quarantine and obtain COVID-19 testing."

Clin Infect Dis: [Transmission of SARS-CoV-2 on a Patient Transport Van](#) (24 April 2021)

"We report 2 episodes of potential SARS-CoV-2 transmission from infected van drivers to passengers despite masking and physical distancing. Whole genome sequencing confirmed relatedness of driver and passenger SARS-CoV-2. With the heater operating, fluorescent microspheres were transported by airflow >3 meters from the front to the back of the van."

Int J Infect Dis: [Isolation of SARS-CoV-2 from the air in a car driven by a COVID patient with mild illness](#) (23 April 2021)

"Objective: To determine if viable virus could be isolated from the air within a car driven by a patient infected with SARS-CoV-2, and to assess the size range of the infectious particles.

Methods: We used a Sioutas personal cascade impactor sampler (PCIS) to screen for SARS-CoV-2 in a car driven by a COVID-19 patient. The patient, who had only mild illness without fever or cough and was not wearing a mask, drove the car for 15 minutes with the air conditioning turned on and windows closed. The PCIS was clipped to the sun-visor above the front passenger seat and was retrieved from the car two hours after completion of the drive.

Results: SARS-CoV-2 was detectable at all PCIS stages by PCR and was cultured from the section of the sampler collecting particles in the 0.25 to 0.50 μm size range.

Conclusions: Our data highlight the potential risk of SARS-CoV-2 transmission by minimally symptomatic persons in the closed space inside of a car and suggest that a substantial component of that risk is via aerosolized virus."

Impact on: HCWs and GME

News in Brief

"Burnout: the crisis plaguing health care workers" ([NPR](#)).

Peer-Reviewed Articles

JAMA Surg: [Factors Associated With General Surgery Residents' Operative Experience During the COVID-19 Pandemic](#) (30 April 2021)

"Question How did general surgery resident operative volume change during the first 4 months of the US COVID-19 pandemic, and were all postgraduate year levels equally affected?

Findings In this review of 1358 resident case logs, general surgery resident operative volume declined by 33.5% in March to June 2020 compared with March to June 2018 and 2019 and affected residents in every level of training.

Meaning These findings illustrate the significant negative effect of the COVID-19 pandemic on general surgery resident operative experience, highlighting the importance of identifying future mitigation strategies."

JMIR Med Educ: [Telemedicine: The Next Frontier for Medical Educators](#) (29 April 2021)

"The COVID-19 pandemic has pushed telemedicine to the forefront of health care delivery, and for many clinicians, virtual visits are the new normal. Although telemedicine has allowed clinicians to safely care for patients from a distance during the current pandemic, its rapid adoption has outpaced clinician training and development of best practices. Additionally, telemedicine has pulled trainees into a new virtual education environment that finds them oftentimes physically separated from their preceptors. Medical educators are challenged with figuring out how to integrate learners into virtual workflows while teaching and providing patient-centered virtual care. In this viewpoint, we review principles of patient-centered care in the in-person setting, explore the concept of patient-centered virtual care, and advocate for the development and implementation of patient-centered telemedicine competencies. We also recommend strategies for teaching patient-centered virtual care, integrating trainees into virtual workflows, and developing telemedicine curricula for graduate medical education trainees by using our TELEMEDS framework as a model."

JAMA Netw Open: [Trends in US Internal Medicine Residency and Fellowship Applications During the COVID-19 Pandemic vs Previous Years](#) (28 April 2021)

"This cross-sectional study evaluates the number of applicants and number of applications submitted per applicant to internal medicine residency and subspecialty fellowships for 2021 compared with 5 prior application cycles."

Acad Med: [ALiEM Connect: Large-Scale, Interactive Virtual Residency Programming in Response to COVID-19](#) (20 April 2021)

"Problem: The COVID-19 pandemic restricted in-person gatherings, including residency conferences. The pressure to quickly reorganize educational conferences and convert content to a remote format overwhelmed many programs. This article describes the pilot event of a large-scale, interactive virtual educational conference model designed and implemented by Academic Life in Emergency Medicine (ALiEM), called ALiEM Connect.

Approach: The pilot ALiEM Connect event was conceptualized and implemented within a 2-week period in March 2020. The pilot was livestreamed via a combination of Zoom and YouTube and was archived by YouTube. Slack was used as a backchannel to allow interaction with other participants and engagement with the speakers (via moderators who posed questions from the backchannel to the speakers live during the videoconference).

Outcomes: The RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework was used for program evaluation, showing that 64 U.S. Accreditation Council for Graduate Medical Education-accredited emergency medicine residency programs participated in the pilot event, with 1,178 unique users during the event (reach). For effectiveness, 93% (139/149) of trainees reported the pilot as enjoyable and 85% (126/149) reported it was equivalent to or better than their usual academic proceedings. Adoption for ALiEM Connect was fairly good with 64/237 (27%) of invited residency programs registering and participating in the pilot event. Implementation was demonstrated by nearly half of the livestream viewers (47%, 553/1,178) interacting in the backchannel discussion, sending a total of 4,128 messages in the first 4 hours.

Next steps: The final component of the RE-AIM framework, maintenance, will take more time to evaluate. Further study is required to measure the educational impact of events like the ALiEM Connect pilot. The ALiEM Connect model could potentially be used to replace educational conferences that have been cancelled or to implement and/or augment a large-scale, shared curriculum among residency programs in the future."

Reinfections, Coinfection, and Other Infectious Diseases

News in Brief

"Malaria vaccine shows promise — now come tougher trials: Preliminary results suggest the vaccine is up to 77% effective in young children, but researchers await larger studies" ([Nature](#)).

Blame Peru's resurgence of tuberculosis on the pandemic ([Undark](#)).

A bit of good news: the flu basically disappeared, thanks in part to the public health measures to slow the coronavirus ([Sci Am](#)).

The WHO has declared most recent Ebola outbreak in the DRC over ([WHO](#)).

Long read: "Scientists scour the Amazon for pathogens that could spark the next pandemic" ([Science](#)).

Special Reports and Other Resources

Resolve: [Epidemics That Didn't Happen: An Original Data Story](#) (accessed 03 May 2021)

10-chapter report, including case studies, interactive features, videos, and more. For a quick summary, see this [STATnews article](#).

"In this report, we share inspiring stories of Epidemics That Didn't Happen, or whose impact was lessened, because of careful planning and swift strategic action. These Epidemics That Didn't Happen show us how the trajectory of an epidemic can be fundamentally altered when a country invests in and prioritizes preparedness for infectious disease outbreaks and readiness to act when it strikes.

As the world continues to work to stop COVID-19 and better prepare for the next disease threat, these stories serve as a reminder that we can do better. By investing in and prioritizing preparedness and response systems, we can save millions of lives and trillions of dollars and avert global tragedy in the years to come.

The COVID-19 pandemic revealed gaps in response systems across high, middle- and low-income countries – it is vital leaders across the world assess, and more importantly, improve, governance for public health emergencies. These examples demonstrate that preparedness works."

Peer-Reviewed Articles

PLoS One: [Evaluation of potential COVID-19 recurrence in patients with late repeat positive SARS-CoV-2 testing](#) (04 May 2021)

"Background: SARS-CoV-2 reinfection and reactivation has mostly been described in case reports. We therefore investigated the epidemiology of recurrent COVID-19 SARS-CoV-2.

Methods: Among patients testing positive for SARS-CoV-2 between March 11 and July 31, 2020 within an integrated healthcare system, we identified patients with a recurrent positive SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) assay ≥ 60 days after an initial positive test. To assign an overall likelihood of COVID-19 recurrence, we combined quantitative data from initial and recurrent positive RT-PCR cycle thresholds—a value inversely correlated with viral RNA burden—with a clinical recurrence likelihood assigned based on independent, standardized case review by two physicians. "Probable" or "possible" recurrence by clinical assessment was confirmed as the final recurrence likelihood only if a cycle threshold value obtained ≥ 60 days after initial testing was lower than its preceding cycle threshold or if the patient had an interval negative RT-PCR.

Results: Among 23,176 patients testing positive for SARS-CoV-2, 1,301 (5.6%) had at least one additional SARS-CoV-2 RT-PCR assay ≥ 60 days later. Of 122 testing positive, 114 had sufficient data for evaluation. The median interval to the recurrent positive RT-PCR was 85.5 (IQR 74–107) days. After combining clinical and RT-PCR cycle threshold data, four patients (3.5%) met criteria for probable COVID-19 recurrence. All four exhibited symptoms at recurrence and three required a higher level of medical care compared to their initial diagnosis. After including six additional patients (5.3%) with possible recurrence, recurrence incidence was 4.3 (95% CI 2.1–7.9) cases per 10,000 COVID-19 patients.

Conclusions: Only 0.04% of all COVID-19 patients in our health system experienced probable or possible recurrence; 90% of repeat positive SARS-CoV-2 RT-PCRs were not consistent with true recurrence. Our pragmatic approach combining clinical and quantitative RT-PCR data could aid assessment of COVID-19 reinfection or reactivation by clinicians and public health personnel."

Clin Infect Dis: [Changes in Seasonal Respiratory Illnesses in the United States During the COVID-19 Pandemic](#) (29 April 2021)

"We categorized emergency department (ED) visits reported to the National Syndromic Surveillance Program according to chief complaints and diagnosis codes, excluding visits with diagnosed SARS-CoV-2 infections. For each week during March 1, 2020 through December 26, 2020 ("pandemic period"), we compared the proportion of ED visits in each respiratory category with the proportion of visits in that category during the corresponding weeks of 2017–2019 ("pre-pandemic period"). We analyzed positivity of respiratory viral tests from two independent clinical laboratories.

During March 2020, cough, shortness of breath, and influenza-like illness accounted for twice as many ED visits compared with the pre-pandemic period. During the last four months of 2020, all respiratory conditions, except shortness of breath, accounted for a

smaller proportion of ED visits than during the pre-pandemic period. Percent positivity for influenza virus, respiratory syncytial virus, human parainfluenza virus, adenoviruses, and human metapneumovirus were lower in 2020 than 2019. Although test volume decreased, percent positivity was higher for rhinovirus/enterovirus during the final weeks of 2020 compared with 2019; with ED visits similar to the pre-pandemic period.

Broad reductions in respiratory test positivity and respiratory emergency department visits (excluding COVID-19) occurred during 2020. Interventions for mitigating spread of SARS-CoV-2 likely also reduced transmission of other pathogens. Timely surveillance is needed to understand community health threats, particularly when current trends deviate from seasonal norms."

Clin Infect Dis: [Sequence Characteristics of COVID-19 Persistence and Reinfection](#) (27 April 2021)

"Background: Both SARS-CoV-2 reinfection and persistent infection have been reported, but sequence characteristics in these scenarios have not been described. We assessed published cases of SARS-CoV-2 reinfection and persistence, characterizing the hallmarks of reinfecting sequences and the rate of viral evolution in persistent infection.

Methods: A systematic review of PubMed was conducted to identify cases of SARS-CoV-2 reinfection and persistence with available sequences. Nucleotide and amino acid changes in the reinfecting sequence were compared to both the initial and contemporaneous community variants. Time-measured phylogenetic reconstruction was performed to compare intra-host viral evolution in persistent SARS-CoV-2 to community-driven evolution.

Results: Twenty reinfection and nine persistent infection cases were identified. Reports of reinfection cases spanned a broad distribution of ages, baseline health status, reinfection severity, and occurred as early as 1.5 months or >8 months after the initial infection. The reinfecting viral sequences had a median of 17.5 nucleotide changes with enrichment in the ORF8 and N genes. The number of changes did not differ by the severity of reinfection and reinfecting variants were similar to the contemporaneous sequences circulating in the community. Patients with persistent COVID-19 demonstrated more rapid accumulation of sequence changes than seen with community-driven evolution with continued evolution during convalescent plasma or monoclonal antibody treatment.

Conclusions: Reinfecting SARS-CoV-2 viral genomes largely mirror contemporaneous circulating sequences in that geographic region, while persistent COVID-19 has been largely described in immunosuppressed individuals and is associated with accelerated viral evolution."

Vaccine: [The impact of disruptions caused by the COVID-19 pandemic on global polio eradication](#) (27 April 2021)

"In early 2020, the COVID-19 pandemic led to substantial disruptions in global activities. The disruptions also included intentional and unintentional reductions in health services, including immunization campaigns against the transmission of wild poliovirus (WPV) and persistent serotype 2 circulating vaccine-derived poliovirus (cVDPV2). Building on a recently updated global poliovirus transmission and Sabin-strain oral poliovirus vaccine (OPV) evolution model, we explored the implications of immunization disruption and restrictions on human interactions (i.e., population mixing) on the expected incidence of polio and on the resulting challenges faced by the Global Polio Eradication Initiative (GPEI). We demonstrate that with some resumption of activities in the fall of 2020 to respond to cVDPV2 outbreaks and full resumption on January 1, 2021 of all polio immunization activities to pre-COVID-19 levels, the GPEI could largely mitigate the impact of COVID-19 to the delays incurred. The relative importance of reduced mixing leading to potentially decreased incidence and reduced immunization leading to potentially increased expected incidence depends on the timing of the effects. Following resumption of immunization activities, the GPEI will likely face similar barriers to eradication of WPV and elimination of cVDPV2 as before COVID-19. The disruptions from the COVID-19 pandemic may further delay polio eradication due to indirect effects on vaccine and financial resources."

Clin Infect Dis: [Re-infection with SARS-CoV-2 in Patients Undergoing Serial Laboratory Testing](#) (25 April 2021)

"Background: A better understanding of re-infection after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has become one of the healthcare priorities in the current pandemic. We determined the rate of re-infection, associated factors and mortality during follow up in a cohort of patients with SARS-CoV-2 infection.

Methods: We analyzed 9,119 patients with SARS-CoV-2 infection who received serial tests in total of 62 healthcare facilities in United States between December 1, 2019 to November 13, 2020. Re-infection was defined by two positive tests separated by interval of greater than 90 days two after resolution of first infection was confirmed by two or more consecutive negative tests. We performed logistic regression analysis to identify demographic and clinical characteristics associated with re-infection.

Results: Re-infection was identified in 0.7% (n=63, 95% confidence interval [CI] 0.5%-0.9%) during follow up of 9,119 patients with SARS-CoV-2 infection. The mean period (\pm standard deviation [SD]) between two positive tests was 116 ± 21 days. A logistic regression analysis identified that asthma (odds ratio [OR] 1.9, 95% CI 1.1-3.2) and nicotine dependence/tobacco use (OR 2.7, 95% CI 1.6-4.5) were associated with re-infection. There was a significantly lower rate of pneumonia, heart failure, and acute kidney injury observed

with re-infection compared with primary infection among the 63 patients with re-infection. There were two deaths (3.2%) associated with re-infection.

Conclusions: We identified a low rate of re-infection confirmed by laboratory tests in a large cohort of patients with SARS-CoV-2 infection. Although re-infection appeared to be milder than primary infection, there was associated mortality."

Viruses: [Mitigating Future Respiratory Virus Pandemics: New Threats and Approaches to Consider](#) (08 April 2021)

"Despite many recent efforts to predict and control emerging infectious disease threats to humans, we failed to anticipate the zoonotic viruses which led to pandemics in 2009 and 2020. The morbidity, mortality, and economic costs of these pandemics have been staggering. We desperately need a more targeted, cost-efficient, and sustainable strategy to detect and mitigate future zoonotic respiratory virus threats. Evidence suggests that the transition from an animal virus to a human pathogen is incremental and requires a considerable number of spillover events and considerable time before a pandemic variant emerges. This evolutionary view argues for the refocusing of public health resources on novel respiratory virus surveillance at human–animal interfaces in geographical hotspots for emerging infectious diseases. Where human–animal interface surveillance is not possible, a secondary high-yield, cost-efficient strategy is to conduct novel respiratory virus surveillance among pneumonia patients in these same hotspots. When novel pathogens are discovered, they must be quickly assessed for their human risk and, if indicated, mitigation strategies initiated. In this review, we discuss the most common respiratory virus threats, current efforts at early emerging pathogen detection, and propose and defend new molecular pathogen discovery strategies with the goal of preempting future pandemics."

Statistics

Global

07 MAY 2021: 156,176,138 confirmed cases and 3,258,680 deaths in 192 countries/regions

Past Trends

30 APR 2021: 150,630,922 confirmed cases and 3,168,601 deaths
 23 APR 2021: 144,878,978 confirmed cases and 3,075,042 deaths
 16 APR 2021: 139,244,306 confirmed cases and 2,989,173 deaths
 09 APR 2021: 134,102,467 confirmed cases and 2,905,149 deaths
 02 APR 2021: 129,761,773 confirmed cases and 2,830,059 deaths
 26 MAR 2021: 125,629,394 confirmed cases and 2,757,473 deaths
 19 MAR 2021: 122,063,523 confirmed cases and 2,695,511 deaths
 12 MAR 2021: 118,719,900 confirmed cases and 2,632,147 deaths
 05 MAR 2021: 115,760,047 confirmed cases and 2,571,789 deaths
 26 FEB 2021: 113,111,157 confirmed cases and 2,510,125 deaths
 19 FEB 2021: 110,439,431 confirmed cases and 2,444,329 deaths
 12 FEB 2021: 107,897,155 confirmed cases and 2,370,870 deaths
 05 FEB 2021: 105,006,686 confirmed cases and 2,287,129 deaths
 29 JAN 2021: 101,605,084 confirmed cases and 2,194,204 deaths in 192 countries/regions
 22 JAN 2021: 97,645,892 confirmed cases and 2,094,191 deaths
 15 JAN 2021: 93,275,676 confirmed cases and 1,997,704 deaths
 08 JAN 2021: 88,203,229 confirmed cases and 1,901,510 deaths in 191 countries/regions

United States

top 5 states by cases

	TOTAL US	CA	TX	FL	NY	IL
Cases	32,606,066	3,753,173	2,909,076	2,258,433	2,064,530	1,348,067
Deaths	580,068	62,154	50,527	35,549	52,572	24,740

[JHU CSSE](#) as of 1000 EDT 07 May 2021

Virginia	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	665,332	20,795	10,376	13,861	17,521	9,003	7,871	35,673
Hospitalizations	28,820	986	362	430	977	669	436	1,590
Deaths	10,874	292	175	224	256	191	187	391

[VA DOH](#) as of 1000 EDT 07 May 2021